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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/312,351	05/14/1999	JON A. WOLFF	MIRUS.006	2480

7590 10/15/2002
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EXAMINER

WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 10/15/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

File

Advisory ActionApplication No.
09/312,351Applicant(s)
Wolff et al.Examiner
Joseph T. WoitachArt Unit
1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED Oct 4, 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
- b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will not be entered because:
- (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see NOTE below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See attached.

3. ☐ Applicant's reply has overcome the following rejection(s): _____
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See attached.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☒ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
- The status of the claim(s) is (or will be) as follows:
- Claim(s) allowed: _____
- Claim(s) objected to: _____
- Claim(s) rejected: 7-11 and 19-28
- Claim(s) withdrawn from consideration: 1-6 and 15-17
8. ☐ The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
10. ☐ Other: _____

DEBORAH CROUCH
PRIMARY EXAMINER

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Applicants' after final amendment filed October 4, 2002, paper number 19, has been received.

Section 2(c):

The proposed amendments to claims 7 and 24 introduce new limitations not previously recited nor specifically considered. The proposed amendments introduce additional molecules which are covalently linked to either side of the disulfide bond. It appears that the compounds in the Pierce catalog do not anticipate each of the newly proposed limitations, however a new search and consideration of the art where the compounds sold by Pierce were used to cross link molecules would have to be evaluated. For example, a teaching wherein the compounds taught by Pierce were used to radiolabel a protein. A more specific example would be a teaching wherein a composition comprising an iodinated hetero-bifunctional crosslinker attached to a protein through its cysteine (i.e. I^{125} -x-S-S-cys-protein) would have to be searched and evaluated.

Section 5(c):

Applicants' comments and arguments presented in the after final amendment, pages 4-7, have been fully considered, but not found persuasive. Initially, it is noted that Examiner appreciates and agrees with the detailed summary of the stability of disulfide bonds. However, it is noted that the comments and arguments are directed to stability and affected trends of pKa's of various thiol groups, and because the proposed amendments have not been entered, these

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arguments are not found persuasive because the compounds taught by Pierce anticipate the pending claims. Further, it appears that the compounds taught in Apricco *et al.* which use the hetero-bifunctional crosslinker to generate an antibody-gelonin molecule would anticipate the compositions in the instantly proposed claims (see for example in schemes 3 and 4).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Pauline Farrier whose telephone number is (703)305-3550.

Joseph T. Woitach